

PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**  
(Case No. 98,365-B1)

In the application of:

<b>Kathleen E. Rodgers, et al.</b>	)	
	)	
Serial No: <b>To be assigned</b>	)	Art Unit: <b>To be assigned</b>
	)	
Filed: <b>Herewith</b>	)	
	)	Examiner: <b>To be assigned</b>
For: <b>Methods for Accelerating Bone, Cartilage,</b>	)	
<b>and Connective Tissue Growth</b>	)	

**Preliminary Amendment**

Assistant Commissioner for Patents  
Washington, D.C. 20231-9999

Dear Sir:

Please enter the following preliminary amendments to the specification and claims:

*In the Specification:*

Please delete lines 6-8 on page 1 and substitute the following: "This application is a continuation of U.S. Patent Application Serial No. 09/352,191 filed July 12, 1999, which claims priority from U.S. Patent Application Serial Nos. 60/092,653 filed July 13, 1998 and 60/130,855 filed April 22, 1999."

*In the claims:*

*Please cancel claims 1-48 without prejudice to their filing in a subsequent continuation application*

49. A method for treating or preventing a bone disorder that results in weakened bones, comprising the administration of an amount effective for treating or preventing a bone disorder in a patient in need thereof at least one active agent comprising a sequence

of at least three contiguous amino acids of groups R<sup>1</sup>-R<sup>8</sup> in the sequence of general formula I



wherein R<sup>1</sup> is selected from H, Asp, Glu, Asn, Acpc (1-aminocyclopentane carboxylic acid), Ala, Me<sup>2</sup>Gly, Pro, Bet, Glu(NH<sub>2</sub>), Gly, Asp(NH<sub>2</sub>) and Suc,

R<sup>2</sup> is selected from Arg, Lys, Ala, Orn, Citron, Ser(Ac), Sar, D-Arg and D-Lys;

R<sup>3</sup> is selected from the group consisting of Val, Ala, Leu, norLeu, Ile, Gly, Pro, Aib, Acpc and Tyr;

R<sup>4</sup> is selected from the group consisting of Tyr, Tyr(PO<sub>3</sub>)<sub>2</sub>, Thr, Ala, Ser, homoSer and azaTyr;

R<sup>5</sup> is selected from the group consisting of Ile, Ala, Leu, norLeu, Val and Gly;

R<sup>6</sup> is selected from the group consisting of His, Arg or 6-NH<sub>2</sub>-Phe;

R<sup>7</sup> is selected from the group consisting of Pro or Ala; and

R<sup>8</sup> is selected from the group consisting of Phe, Phe(Br), Ile and Tyr; excluding sequences including R<sup>4</sup> as a terminal Tyr group, or is absent.

50. The method of claim 49 wherein the active agent comprises at least four contiguous amino acids of general formula I.

51. The method of claim 49 wherein the active agent comprises at least five contiguous amino acids of general formula I.

52. The method of claim 49 wherein the active agent comprises at least six contiguous amino acids of general formula I.

53. The method of claim 49 wherein the active agent comprises at least seven contiguous amino acids of general formula I.

54. The method of claim 49 wherein the active agent comprises an amino acid sequence selected from the group consisting of angiotensinogen, SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID

NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO: 32, SEQ ID NO:33, SEQ ID NO: 34; SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45.

55. The method of claim 49 wherein the active agent comprises an amino acid sequence selected from the group consisting of angiotensinogen, SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO: 32, SEQ ID NO:33, SEQ ID NO: 34; SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45.

56. The method of claim 49 wherein the active agent comprises an amino acid sequence selected from the group consisting of angiotensinogen, SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:8, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO: 32, SEQ ID NO:33, SEQ ID NO: 34; SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45, wherein the active agent does not consist essentially of SEQ ID NO:1.

57. The method of claim 49 wherein the active agent consists of at least three contiguous amino acids of general formula I.

58. The method of claim 49 wherein the active agent consist of at least four contiguous amino acids of general formula I.

59. The method of claim 49 wherein the active agent consist of at least five contiguous amino acids of general formula I.
60. The method of claim 49 wherein the active agent consist of at least six contiguous amino acids of general formula I.
61. The method of claim 49 wherein the active agent consist of at least seven contiguous amino acids of general formula I.
62. The method of claim 49 wherein the active agent consists of an amino acid sequence selected from the group consisting of angiotensinogen, SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO: 32, SEQ ID NO:33, SEQ ID NO: 34; SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45.
63. The method of claim 49 wherein the active agent consists of an amino acid sequence selected from the group consisting of angiotensinogen, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO: 32, SEQ ID NO:33, SEQ ID NO: 34; SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45.
64. The method of claim 49 wherein the active agent consists of an amino acid sequence selected from the group consisting of angiotensinogen, SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:8, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ

ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34; SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45.

65. The method of claim 49 wherein the active agent does not consist of SEQ ID NO:1.

66. The method of any of claims 49-65, wherein the bone disorder that results in weakened bones is selected from the group consisting of osteoporosis, osteoarthritis, Paget's disease, osteohalisteresis, osteomalacia, periodontal disease, bone loss resulting from cancer, bone loss resulting from steroid use, and age-related loss of bone mass.

### **SUPPORT FOR THE NEW CLAIMS**

Claims directed towards using the active agents for treating or preventing a bone disorder that results in weakened bones, including the specific conditions cited in claim 66, are supported throughout the application, for example on page 8 lines 11-19; page 8 line 22 to page 9 line 3; and page 34 lines 6-12. Thus, the new claims do not constitute new matter.

### **Co-pending applications**

The Applicants hereby notify the Examiner of the following commonly owned, co-pending applications that relate to the use of the active agents for other purposes:

97,016-C	09/434,746	11/5/99
97,017-F1	09/198,806	11/24/98
97,017-G	09/012,400	1/23/98
97,017-G2	09/564,051	5/3/00
97,017-G3	09/564,045	5/3/00
97,017-K1	09/264,563	3/8/99
97,017-M1	09/287,674	4/7/99
97,017-P1	09/307,940	5/10/99

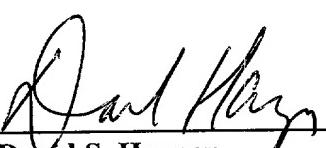
97,017-P7	09/723,197	11/27/00
97,017-P8	09/716,394	11/27/00
98,008-A	09/255,136	2/19/99
98,009-B	09/245,680	2/8/99
98,009-B1	09/658,315	9/8/00
98,010-A	09/250,703	2/16/99
98,028-A	09/246,525	2/8/99
98,094-B1	09/332,582	6/14/99
98,364-A	09/373,962	8/13/99
98,364-A1	09/657,890	9/8/00
98,365-B	09/352,191	7/12/99
99,1043-A	to be assigned	1/26/01
99,165-A	09/532,221	3/22/00
99,931-A	09/723,024	11/27/00
99,933-B	09/723,257	11/27/00
00,1128-A	09/698,354	10/27/00
00,1188-E	09/608,532	6/30/00
00-1188-E1	09/723,437	11/28/00
00,1222-B	09/503,872	2/14/00
00,448-A	09/723,255	11/27/00

If there is any problem, the examiner is respectfully invited to call the below signed attorney at (312) 913-2106.

Respectfully submitted,

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Date: 1-30-01

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